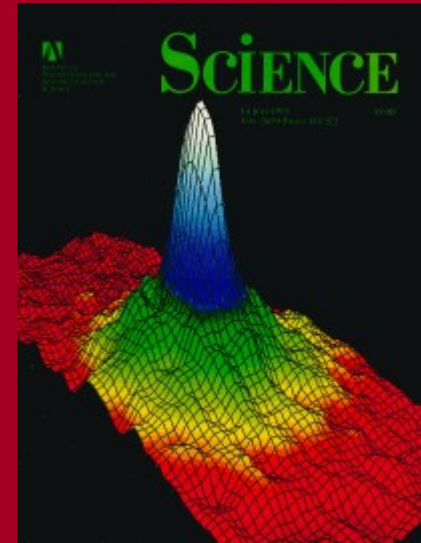


# Outlining a CONSORT statement

Methods – Extension to biobank studies

# Context

**Epidemiology faces its limits**  
(Taubes, 1995)



June 22,  
2000

**Randomized Trials or Observational Tribulations?**  
(Pocock & Elbourne)

**A Comparison of Observational Studies and  
Randomized, Controlled Trials** (Benson & Hartz)

**Randomized, Controlled Trials, Observational  
Studies, and the Hierarchy of Research Designs**  
(Concato, Shah & Horwitz)

# Context

**Beyond randomised versus observational studies**  
(Concato & Horwitz)

**Those confounded vitamins: what can we learn from the differences between observational versus randomised trial evidence?** (Lawlor et al.)

**When are observational studies as credible as randomised trials?** (Vandenbroucke)



22 May, 2004



6 October, 2004

**The scandal of poor epidemiological research**  
*Reporting guidelines are needed for observational epidemiology* (von Elm & Egger)

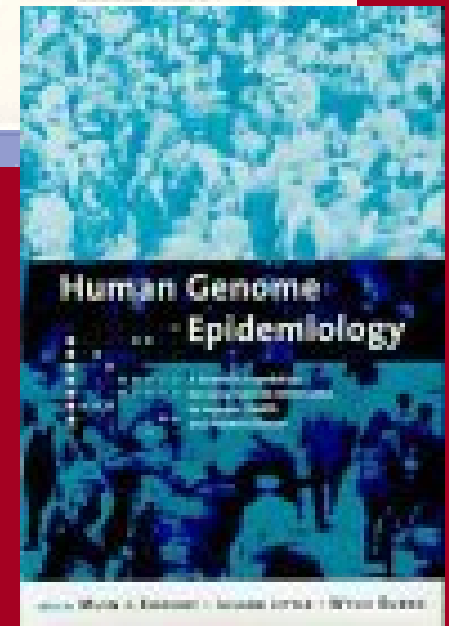
**Issues in the reporting of epidemiological studies: a survey of recent practice**  
(Pocock et al.)

# Reporting and Review of Human Genome Epidemiology Studies

- Selection of study subjects
- Analytic validity of genotyping
- Assessment of exposure
- Confounding, including population stratification
- Statistical issues

Reporting, Appraising, and Integrating Data on Genotype Prevalence and Gene-Disease Associations *Am J Epidemiol* 2002;156:300–10.

Reporting and Review of Human Genome Epidemiology Studies. In: Khoury MJ, Little J, Burke W. (Editors). *Human Genome Epidemiology: A scientific foundation for using genetic information to improve health and prevent disease*. New York, Oxford University Press, 2004, pp. 168-192.



# Checklists for non-randomized evaluations of interventions

## Evaluating non-randomised intervention studies (Deeks et al., 2003)

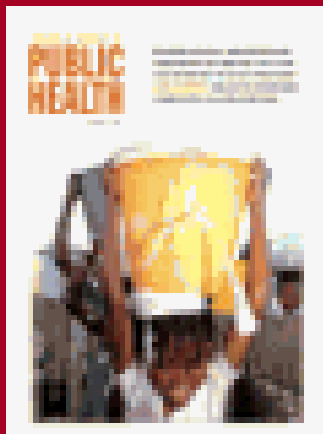
“Although many quality assessment tools exist and have been used for appraising non-randomised studies, most omit key quality domains.”



## Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement.

(Des Jarlais et al., 2004)

**TREND: Transparent Reporting of Evaluations with Nonrandomized Designs**



# Checklists relating to cohort studies



**SIGN 50:**  
**A guideline developers' handbook**  
**SIGN Publication No. 50, 2001**  
**(updated 2004)**

**<http://www.sign.ac.uk/guidelines/fulltext/50/index.html>**

**Annex C. Critical appraisal: Notes and checklists**  
**Methodology Checklist 3: Cohort Studies**



**Tooth L et al. Quality of Reporting of Observational Longitudinal Research. *Am J Epidemiol* 2005; 161: 280-8.**

# Draft methods checklist – single studies (following CONSORT layout)

## Participants

*Initial enrolment*

**Eligibility criteria** for participants (includes methods of recruitment)

**Settings and locations** where the data were collected

**\*Ethnic group**

**\*Recruitment from families** (e.g. twin pairs, index births and their parents)

*\*Nested studies*

**Design** – nested case-control, nested case-cohort, nested case-only

\*potential issues requiring particular consideration in biobank studies

# Draft methods checklist – single studies (following CONSORT layout)

	Types of samples used†
<del>Interventions</del>	Timing of sample collection and analysis†*
<del>Genotyping</del>	Success rate in extracting DNA†*
	Definition of the genotype(s) investigated; when there are multiple alleles, those tested for should be specified
	Genotyping method used (reference; for PCR methods – primer sequences*, thermocycle profile*, number of cycles*)

† Are there differences by study group, e.g. exposure status at enrolment, or in nested studies, between cases and non-cases?

\*Additional information recorded (ideally in web-based methods register)



# Draft methods checklist – single studies (following CONSORT layout)

## ~~Interventions~~

Quality control measures, including blinding of laboratory staff (to exposure; to outcome in nested studies)†\*#

## Genotyping contd.

Samples from each group of subjects compared (e.g. cases and non-cases in nested study) included in each batch analyzed\*

† Are there differences by study group, e.g. exposure status at enrolment, or in nested studies, between cases and non-cases?

\* Additional information recorded (ideally in web-based methods register)

# See specific heading on blinding (masking)

# Draft methods checklist – single studies (following CONSORT layout)

## ~~Interventions~~

Methods of assessing exposures documented†

## Exposure assessment

- primary exposures and confounders identified when biobank initiated
- more detailed assessments in nested studies (N.B. recall bias)

Reproducibility and validity of exposure documented

Categories or exposure scale justified

† Are there differences by study group, e..g. exposure status at enrolment, or in nested studies, between cases and non-cases?

# Draft methods checklist – single studies (following CONSORT layout)

**Objectives**      *Specific objectives and hypotheses.*

In biobank study, a major objective (and undertaking!) is establishing the biobank itself.

Some specific objectives and hypotheses formulated *a priori* (for funding agencies; depending on interests of investigators).

Others are likely to be added over time, e.g. as a result of new collaborations. These would be *a priori* hypotheses in the sense that they are not data driven, but may be secondary in the sense that the biobank was not specifically designed to test them.

# Draft methods checklist – single studies (following CONSORT layout)

## **Objectives** contd.

*Specific objectives and hypotheses*

Potential combination of:

- assessment of large number of genotypes (enabled by high throughput genotyping)
- assessment of large number of exposures assessed at multiple time points
- multiple outcomes

# Draft methods checklist – single studies (following CONSORT layout)

**Outcomes**      *Clearly defined primary and secondary outcome measures*

Compared with RCT, broader range of disease outcomes likely to be assessed in a biobank study (but information about potential complications of intervention, QoL, patient-borne costs unlikely to be sought)

Scale of biobank studies means methods of outcome assessment likely to be less detailed than in RCT, e.g.

- “passive” methods of ascertainment likely to be used, e.g. linkage to cancer registration, hospital discharge data systems, vital records
- self report (positive reports verified by chart abstraction; possibly a sample of negative reports)

# Draft methods checklist – single studies (following CONSORT layout)

## **Outcomes**

contd.

*When applicable, any methods used to enhance the quality of measurements (eg, multiple observations, training of assessors).*

# Draft methods checklist – single studies (following CONSORT layout)

**Sample size** *How sample size was determined*

Applies to

- overall design of biobank
- nested studies

# Draft methods checklist – single studies

(following CONSORT layout)

**Randomization**

**Confounding**

Factors associated with the outcome and exposure under investigation (that are not an intermediate step between exposure and outcome) – data collected and potential confounding assessed in analysis

Alleles associated with the outcome in linkage disequilibrium with the allele under investigation taken into account



# Draft methods checklist – single studies

(following CONSORT layout)

**Randomization**

*Population stratification:*

- Unaccounted variation in ethnic backgrounds by exposure group when ethnic groups tend to have different exposures and different frequencies of allelic variants

**Confounding**

- In nested case-control study, unaccounted variation in ethnic backgrounds of cases and controls, when ethnic groups have different rates of outcome and different frequencies of allelic variants

# Draft methods checklist – single studies (following CONSORT layout)

## ~~Randomization~~

### *Population stratification:*

So far, empirical evidence in populations of European origin suggests magnitude of any bias small (Wacholder et al., 2000; Ardlie et al., 2002; Freedman et al., 2004; Khlat et al., 2004; Wang et al., 2004)

## Confounding

Interpretation of empirical evidence for African American populations mixed (Millikan et al., 2001; Ardlie et al., 2002; Freedman et al., 2004)

Likely to be less of a problem for cohort studies and studies nested within them than for case-control studies.

# Draft methods checklist – single studies (following CONSORT layout)

## **Blinding (masking)**

Whether or not those assessing the outcomes were blinded to exposure status and genotype.

Whether or not those assessing the genotypes

- blinded to exposure status
- in nested study, blinded to outcome

# Draft methods checklist – single studies (following CONSORT layout)

## Statistical methods

Distinguish clearly *a priori* hypotheses and hypotheses generated

Statistical methods used to

- Assess associations
- Test for gene-exposure interaction

Methods to take account of

- loss to follow-up
- potential confounding
- missing data

Methods (& justification) for additional analyses, such as subgroup analyses